

PATENT COOPERATION TREATY

PCT


10/541346 541,346

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Rec'd PCT/PTO 05 JUL 2005
 REC'D JUN 2005
 WIPO PCT
 05 JUL 2005

Applicant's or agent's file reference		FOR FURTHER ACTION		See Form PCT/PEA/416
International application No. PCT/US2004/002907		International filing date (day/month/year) 02.02.2004	Priority date (day/month/year) 12.02.2003	
International Patent Classification (IPC) or national classification and IPC C12N15/82, C12Q1/68				
Applicant MONSANTO TECHNOLOGY LLC et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 8 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> sent to the applicant and to the International Bureau) a total of 4 sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand 03.09.2004		Date of completion of this report 17.03.2005		
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Pilat, D Telephone No. +49 89 2399-8668		



**INTERNATIONAL PRELIMINARY REPORT
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PCT/US2004/002907

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

Description, Pages

1-31 as originally filed

Claims, Numbers

1-19 filed with telefax on 18.02.2005

Drawings, Sheets

1/5-5/5 as originally filed

- ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-19
	No: Claims	
Inventive step (IS)	Yes: Claims	1-19
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-19
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and /or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

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Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing:
 - ☒ contained in the international application as filed
 - ☒ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
 - ☐ received by this Authority as an amendment on
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional observations, if necessary:

Ad Section I: Basis of the opinion

1. Reference is made to the following documents:

- D1: WO 02/44407 A (ROSQUE INGE ; SES EUROP N V (BE); BARNES STEVE (BE); WEYENS GUY (BE)) 6 June 2002 (2002-06-06)
- D2: US-B-6 462 2581 (FINCHER KAREN L ET AL) 8 October 2002 (2002-10-08)
- D3: PLINE WENDY A ET AL: "Reproductive abnormalities in glyphosate-resistant cotton caused by lower CP4-EPSPS levels in the male reproductive tissue" WEED SCIENCE, vol. 50, no. 4, July 2002 (2002-07), pages 438-447, XP002292800 ISSN: 0043-1745
- D4: WO 02/34946 A (MONSANTO TECHNOLOGY LLC ; YE MINWEI (US); RANGWALA TASNEEM S (US)) 2 May 2002 (2002-05-02)
- D5: MICHAEL A. JONES AND CHARLES E. SNIPES: "Tolerance of Transgenic Cotton to Topical Applications of Glyphosate" JOURNAL OF COTTON SCIENCE, vol. 3, 1999, pages 19-26, XP002292746
- D6: WINDELS P ET AL: "DEVELOPMENT OF A LINE SPECIFIC GMO DETECTION METHOD A CASE STUDY" MEDEDELINGEN VAN DE FACULTEIT LANDBOUWWETENSCHAPPEN UNIVERSITEIT GENT, GENT, BE, vol. 64, no. 5B, 22 September 1999 (1999-09-22), pages 459-462, XP001032975 ISSN: 0368-9697
- D7: WO 02/100163 A (MONSANTO TECHNOLOGY LLC ; HUBER SCOTT A (US); DOHERTY SEAN (US); ROBER) 19 December 2002 (2002-12-19)
- D8: WO 99/46396 A (MONSANTO CO) 16 September 1999 (1999-09-16)
- D9: EP-A-0 899 341 (MYCOGEN CORP) 3 March 1999 (1999-03-03)
- D10 GINGER G. LIGHT ET AL.: "Yield Of Glyphosate-Tolerant Cotton As Affected By Topical Glyphosate Applications On The Texas High Plains And Rolling Plains" JOURNAL OF COTTON SCIENCE, vol. 7, 2003, pages 231-235, XP002292747

2) Amendments (Article 34 PCT)

The amendments introduced in the claims submitted by the applicant appear to be admissible.

***Ad Section V :Reasoned statement under Rule 66.2(a)(ii); citations and explanations
supporting such statement***

2. Novelty (Article 33 (2) PCT)

- 2.1 None of the document cited in the international search report seem to disclose a seed cotton a plant or plant parts as defined in claims 1-6. The same conclusion applies to a DNA primer set as claimed in claims 7-9, to methods of producing a cotton plant comprising sexual crossing a glyphosate tolerant cotton event MON 88913, to the method of detecting a DNA corresponding to said cotton event MON 88913 as claimed in claims 10-15. Similarly a method of determining the zygosity of the progeny of cotton event MON 88913 and a method of controlling weeds in a crop of cotton event MON 88913 as claimed in claims 17-19 seem novel.

3. Inventive step (Article 33 (3) PCT)

- 3.1 Document D4 (WO0234946) is considered to represent the most relevant state of the art. It discloses a commercial cotton event (1445) which provides excellent tolerance to glyphosate through the four-leaf stage but not beyond this stage (see present application p.1 3§).

The difference between claim 1 and this document lies in that claim 1 refers to a different cotton event 88913.

The effect associated with this difference is that said cotton event is more tolerant to glyphosate than the current commercial cotton event (see present application p.19 last §)

The problem to be solved by the present invention may therefore be regarded as to obtain a new cotton event having an increased tolerance to glyphosate.

D5 (Jones et al.) or D4 (WO9946396) or D3 (Pline et al.) state that glyphosate is gametocide. D3 states that CP4 EPSPS in stigma, anther, preanthesis floral bud and flower petals were significantly less than that in the vegetative leaf tissue (see D3 p. 444 col.2 half page and figure 2b). In the light of D3, it becomes apparent that male reproductive organs in glyphosate resistant cotton appears to be only partially resistant to the effects of glyphosate, presumably because of the insufficient

presence of CP4-EPSPS. Thus, the presence of suboptimal quantities of the CP4-EPSPS in these tissues may slow, instead of completely inhibit, pollen maturation (see D3 p.444 col.2 last § and p.446 col.1 last §).

In view of this prior art, the skilled person would have had an incentive to look for an other cotton event, but would not have had a reasonable expectation of success to obtain the cotton event as presently claimed. This solution claimed in claim 1 seems to involve an inventive step. The same conclusion applies for dependent claims or claims referring to said selected cotton event as claimed in claims 2-11,13,14,15,17-19.

Ad section VIII: Certain observations on the international application.

4. Clarity (Article 6 PCT)

- 4.1 From the present description it is unclear whether the deposited MON 88913 is homozygous or heterozygous.
- 4.2 Should the present seed cotton event designated MON 88913 contain a transgenic endosperm and a wild type embryo then the plant or plant parts produced thereof would be undistinguishable from wild type plants or plant parts.
- 4.3 Should the present seed cotton event designated MON 88913 deposited under accession No PTA-4854 be heterozygous, then a pollen or ovule, produced by growing the seed of claim 1 and due to segregation, would possibly be undistinguishable from wild-type cotton pollen or ovule. Claim 3 has to be clarified.
- 4.4 Claim 16 does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claim attempts to define the subject-matter in terms of the result to be achieved which merely amounts to a statement of the underlying problem. At present, it is unclear based on which criteria a glyphosate trait must be considered as genetically linked. Is the same chromosomal location sufficient?
- 4.5 In the European regional phase, the present authority informs that a patent will not be

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granted if the claimed subject-matter is directed to a specific plant variety or specific plant varieties. However, if the invention concerns plants and animals and if the technical feasibility of the invention is not confined to a particular plant or animal variety, the invention would be patentable (Article 53(b) EPC).

5. Support and Description (Article 6 PCT and Rule 5a PCT).

Claim 16 relates to a cotton plant. However, there is no example throughout the whole application as filed for a cotton plant glyphosate having a glyphosate trait except the specific cotton event MON 88913 and its progeny. In this respect, the claimed subject-matter does not appear to be adequately supported.

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Monsanto Technology LLC

11899.0239.00PC00
February 18, 2005

CLAIMS:

1. Seed of cotton event designated MON 88913 comprising SEQ ID NO:1 and SEQ ID NO:2 and having representative seed deposited with American Type Culture Collection (ATCC) with Accession No. PTA-4854.
2. The cotton plant or parts thereof produced by growing the seed of claim 1.
3. The cotton plant or parts thereof of claim 2, comprising pollen, ovule, flowers, bolls, lint, shoots, roots, or leaves.
4. Glyphosate tolerant progeny of the cotton plant of claim 2.
5. A progeny cotton plant of claim 4, wherein the genome of said cotton plant comprises one or more DNA molecules selected from the group consisting of SEQ ID NO: 1, SEQ ID NO:2, SEQ ID NO:3, and SEQ ID NO:4.
6. A progeny cotton plant or seed or parts thereof of claim 4, the genome of which produces an amplicon comprising SEQ ID NO: 1 or SEQ ID NO:2 in a DNA amplification method.
7. A DNA primer set comprising two DNA molecules, wherein the first DNA molecule comprises at least 11 or more contiguous polynucleotides of any portion of the transgene region of the DNA molecule of SEQ ID NO:3 or its complement, and the second DNA molecule of similar length comprises any portion of a 5' flanking cotton genomic DNA region of SEQ ID NO:3 or its complement, where these DNA molecules when used together are useful in a DNA amplification method to produce an amplicon comprising SEQ ID NO: 1 diagnostic for cotton event MON 88913.
8. A DNA primer set comprising two DNA molecules, wherein the first DNA molecule comprises at least 11 or more contiguous polynucleotides of any portion of the transgene region of the DNA molecule of SEQ ID NO:4, or its complement, and the second DNA molecule of similar length comprises any portion of a 3' flanking cotton genomic DNA region of SEQ ID NO:4, or its complement, where these DNA molecules when used together are useful as a DNA primer set in a DNA amplification method to produce an amplicon comprising SEQ ID NO:2 diagnostic for cotton event MON 88913.
9. A DNA detection kit comprising at least one molecule of 11 or more contiguous

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nucleotides homologous or complementary to SEQ ID NO:3 or SEQ ID NO:4, that when used in a DNA amplification methods produces an amplicon comprising SEQ ID NO: 1 or SEQ ID NO:2 diagnostic for cotton event MON 88913.

10. A method of producing a cotton plant that tolerates application of glyphosate herbicide comprising:

(a) sexually crossing a first glyphosate tolerant cotton event MON 88913 parent plant comprising SEQ ID NO:1 and SEQ ID NO:2 and a second parent cotton plant that lacks the tolerance to glyphosate herbicide, thereby

producing a plurality of first progeny plants; and

(b) selecting a first progeny plant that is tolerant to glyphosate; and

(c) selfing said first progeny plant, thereby producing a plurality of second progeny plants; and

(d) selecting from said second progeny plants, a glyphosate tolerant plant.

11. The method of claim 10 further comprising the step of backcrossing the first progeny plant that is tolerant to glyphosate or the second progeny plant that is glyphosate tolerant to the second parent plant or a third parent plant, thereby producing a plant that tolerates the application of glyphosate.

12. A method of detecting the presence of DNA corresponding to cotton event MON 88913 comprising SEQ ID NO:1 and SEQ ID NO:2 in a sample, the method comprising:

(a) contacting the sample comprising DNA with a DNA primer set comprising

(i) at least 11 contiguous nucleotides of a 5' flanking cotton genomic DNA region flanking the insertion site in cotton event MON88913 or its complement, or a 3' flanking cotton genomic DNA region flanking the insertion site in cotton event MON88913 or its complement, and

(ii) at least 11 contiguous nucleotides of the transgene region of SEQ ID NO:3 or SEQ ID NO:4;

which when used in a nucleic acid amplification reaction with genomic DNA from the cotton event MON 88913, produces a diagnostic amplicon comprising SEQ ID NO:1 or SEQ ID NO:2;

and

(b) performing a nucleic acid amplification reaction, thereby producing a sample amplicon;

and

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(c) comparing the sample amplicon to the diagnostic amplicon to determine whether the sample amplicon comprises SEQ ID NO:1 or SEQ ID NO:2.

13. In the method of claim 12, where in said primer set comprises SEQ ID NO:21, SEQ ID NO:22 and SEQ ID NO:24.

14. In the method of claim 12, wherein said primer set comprises SEQ ID NO:26, SEQ ID NO:27 and SEQ ID NO:28.

15. A method of detecting the presence of a DNA corresponding to cotton event MON 88913 in a sample, the method comprising:

(a) contacting the sample comprising DNA with a probe that hybridizes under stringent hybridization conditions with genomic DNA from the cotton event MON 88913, comprising SEQ ID NO:1 and SEQ ID NO:2, and does not hybridize under the stringent hybridization conditions with a control cotton plant genomic DNA, wherein said probe is homologous or complementary to SEQ ID NO:1 or SEQ ID NO:2; and

(b) subjecting the sample and probe to stringent hybridization conditions; and

(c) detecting hybridization of the probe to the DNA.

16. A cotton plant comprising a glyphosate tolerant trait that is genetically linked to a complement of a marker polynucleic acid, wherein said marker polynucleic acid molecule is homologous or complementary to a DNA molecule selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2.

17. A method of determining the zygosity of the progeny of cotton event MON 88913 comprising:

(a) contacting the sample comprising cotton DNA with a primer set comprising SEQ ID NO:21, SEQ ID NO:22 and SEQ ID NO:23, that when used in a nucleic-acid amplification reaction with genomic DNA from cotton event MON 88913, produces a first amplicon that is diagnostic for cotton event MON 88913; and

(b) performing a nucleic acid amplification reaction, thereby producing the first amplicon; and

(c) detecting the first amplicon; and

(d) contacting the sample comprising cotton DNA with said primer set, that when used in a nucleic-acid amplification reaction with genomic DNA from cotton plants produces a

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second amplicon comprising the native cotton genomic DNA homologous to the cotton genomic region of a transgene insertion identified as cotton event MON 88913;

(e) performing a nucleic acid amplification reaction, thereby producing the second amplicon; and

(f) detecting the second amplicon; and

(g) comparing the first and second amplicons in a sample, wherein the presence of both amplicons indicates the sample is heterozygous for the transgene insertion.

18. A method of determining the zygosity of the progeny of cotton event MON 88913 comprising:

(a) contacting the sample comprising cotton DNA with a primer set comprising SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, and SEQ ID NO:25; and

(b) performing a nucleic acid amplification reaction; and

(c) detecting the products of the reaction.

19. A method for controlling weeds in a crop of cotton event MON 88913, comprising SEQ ID NO:1 and SEQ ID NO:2, comprising the step of applying an effective dose of a glyphosate containing herbicide to said crop of cotton event MON 88913.